

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Rene Gantier et al  
Serial No. : 10/658,355  
Filed : September 8, 2003  
Cust. No. : 20985  
Title : RATIONAL DIRECTED PROTEIN EVOLUTION USING TWO-DIMENSIONAL RATIONAL MUTAGENESIS SCANNING

Art Unit : 1631  
Examiner : Russell Scott Negin  
Conf. No. : 3519

**Mail Stop Amendment**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**TRANSMITTAL LETTER**

Dear Sir:

Transmitted herewith are a Supplemental Information Disclosure Statement (5 pages); Form PTO-1449 (2 pages); cited non U.S. patent documents; copies of two European Examination Reports, issued December 6, 2006 and July 31, 2007, in connection with European Patent Application No. 02798018.4; copies of seven U.S. Office Actions issued October 18, 2004; June 15, 2005; December 23, 2005; April 17, 2006; September 7, 2006; May 9, 2007; and August 30, 2007, in connection with U.S. Application Ser. No. 10/022,249; return postcard; and a check for the requisite fee of \$180.00 for filing in connection with the above-captioned patent application.



The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 06-1050. A duplicate of this sheet is enclosed.

Respectfully submitted,

Stephanie Seidman  
Reg. No. 23,779

Attorney Docket No. 17109-013001 / 923

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**CERTIFICATE OF MAILING BY "EXPRESS MAIL"**

"Express Mail" Mailing Label Number EV 965983890 US  
Date of Deposit September 4, 2007.

I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

Stephanie Seidman



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN  
ACCORDANCE WITH 37 C.F.R. §§1.97-1.98**

Dear Sir:

Because this Supplemental Information Disclosure Statement is after receipt of a first Office Action on the Merits of the above-captioned application, the filing fee of \$180 is enclosed. If no proper payment is enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 06-1050.

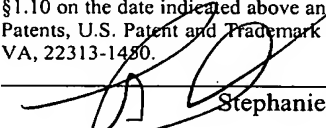
In accordance with the duty of disclosure imposed by 37 C.F.R. §1.56 to inform the Patent Office of all information known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Supplemental Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§1.97-1.98. Form PTO-1449 (3 pages) and copies of the cited non U.S. patent documents are provided herewith in connection with the above-captioned application.

09/07/2007 SSITHIB1 00000039 10658355

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CERTIFICATE OF MAILING BY "EXPRESS MAIL"  
"Express Mail" Mailing Label Number EV 965983890 US  
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I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

  
Stephanie Seidman

The documents listed on the Form PTO-1449 are in the English language. Hence, in accordance with the requirements of 37 C.F.R. §1.98, as amended effective March 16, 1992, no further explanation of the listed items is necessary.

Copies of seven U.S. Office Actions (Documents III-IX), issued October 18, 2004; June 15, 2005; December 23, 2005; April 17, 2006; September 7, 2006; May 9, 2007; and August 30, 2007, respectively, in connection with co-owned U.S. Application Ser. No. 10/022,249 are provided. Copies of two European Examination Reports (Documents I and II), issued December 6, 2006 and July 31, 2007, respectively, in connection with European Patent Application No. 02798018.4 are provided. European Patent Application No. 02798018.4 corresponds to U.S. Application Ser. No. 10/022,249. The table below lists Documents I-IX and includes a column that provides a space next to the documents to be considered, for the Examiner's initials.

Examiner Initial	Document No.	Document
	I	Copy of European Examination Report, issued December 6, 2006, in connection with European Patent Application No. 02798018.4
	II	Copy of European Examination Report, issued July 31, 2007, in connection with European Patent Application No. 02798018.4
	III	Copy of U.S. Office Action, issued October 18, 2004, in connection with U.S. Application Ser. No. 10/022,249
	IV	Copy of U.S. Office Action, issued June 15, 2005, in connection with U.S. Application Ser. No. 10/022,249
	V	Copy of U.S. Office Action, issued December 23, 2005, in connection with U.S. Application Ser. No. 10/022,249
	VI	Copy of U.S. Office Action, issued April 17, 2006, in connection with U.S. Application Ser. No. 10/022,249
	VII	Copy of U.S. Office Action, issued September 7, 2006, in connection with U.S. Application Ser. No. 10/022,249
	VIII	Copy of U.S. Office Action, issued May 9, 2007, in connection with U.S. Application Ser. No. 10/022,249
	IX	Copy of U.S. Office Action, issued August 30, 2007, in connection with U.S. Application Ser. No. 10/022,249

In the European Examination Report, issued December 6, 2006 (Document I), the Examiner cites six documents: 1) WO 01/32844, 2) WO 01/44809, 3) WO 95/23813, 4) WO 01/86291, 5) US 6,013,478 and 6) Drittanti et al., "High throughput production, screening and analysis of adeno-associated viral vectors," *Gene Therapy*, 7(11):924-929 (2000). Documents 1-6 have already been made of record in the instant application in Information Disclosure Statements, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents, filed March 17, 2004, November 9, 2004 and January 20, 2005. In the U.S. Office Action, issued October 18, 2004 (Document III), the Examiner cites one document: 1) US 6,171,820. Document 1 has already been made of record in the instant application in an Information Disclosure Statement, supplied with Forms PTO-1449, filed November 9, 2004. In the U.S. Office Action, issued December 23, 2005 (Document V), the Examiner cites two documents: 1) US 5,925,565 and 2) US 2002/0081574. Documents 1 and 2 have already been made of record in the instant application in an Information Disclosure Statement, supplied with Forms PTO-1449, filed January 4, 2006. In the U.S. Office Action, issued April 17, 2006 (Document VI), the Examiner cites one document: 1) Zlauddin et al., "Microarrays of cells expressing Defined cDNAs," *Nature*, 411:107-110 (2001). Document 1 has already been made of record in the instant application in an Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents, filed July 12, 2006. In the U.S. Office Action, issued September 7, 2006 (Document VII), the Examiner cites two document: 1) Giver et al., "Directed evolution of a thermostable esterase," *PNAS* 95:12809-12813 (1998), and 2) Persson et al., "Virus-receptor interaction in the adenovirus system: characterization of the positive cooperative binding of virions on HeLa cells," *Journal of Virology* 54:92-97 (1985). Documents 1 and 2 have already been made of record in the instant application in an Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents, filed September 26, 2006.

Further to the list provided in the communication filed on November 9, 2006, applicant also makes known to the Examiner the following pending U.S. and International Applications that have one or more common inventors and/or are commonly owned:

<b>U.S.S.N.</b>	<b>Filing Date</b>	<b>Publ. No.</b>	<b>Publ. Date</b>	<b>Docket No.</b>
11/476,173	06/26/06	2006-0247170	11/02/06	925B
11/412,939	04/28/06	2006-0195268	08/31/06	n/a
11/429,100	05/04/06	2006-0251619	11/09/06	926
11/656,921	01/22/07	n/a	n/a	922E
11/703,610	02/06/07	n/a	n/a	922C
11/704,141	02/07/07	n/a	n/a	922D
11/706,088	02/13/07	2007-0172459	07/26/07	922F
11/707,014	02/14/07	n/a	n/a	922G
11/729,267	03/27/07	n/a	n/a	924
11/729,266	03/27/07	n/a	n/a	924B
11/788,836	04/19/07	n/a	n/a	932
11/818,985	06/15/07	n/a	n/a	930
11/825,604	07/05/07	n/a	n/a	922H
<b>Int'l App. No.</b>	<b>Filing Date</b>	<b>Publ No.</b>	<b>Publ. Date</b>	<b>Docket No.</b>
PCT/IB05/003662	11/04/05	WO 06/048777	05/11/06	925PC
PCT/IB06/002034	05/04/06	WO 06/120580	11/16/06	926PC
PCT/EP07/002700	03/27/07	n/a	n/a	924PC
PCT/US07/14219	06/15/07	n/a	n/a	930PC

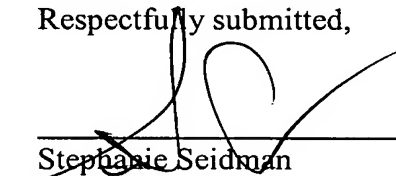
Although these documents and applications are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the information, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. §1.97 (g and h), the filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. §1.56 (b) exists.

Applicant : Rene Gantier et al.  
Serial No. : 10/658,355  
Filed : September 8, 2003

Attorney's Docket No.: 17109-013001 / 923  
Supplemental Information Disclosure Statement

Applicant respectfully requests that the Examiner review the foregoing documents and make them of record in the file history of the above-captioned application.

Respectfully submitted,



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Stephanie Seidman  
Reg. No. 33,779

Attorney Docket No. 17109-013001 / 923

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Substitute Form PTO-1449 (Modified)  <b>List of Patents and Publications for Applicant's Information Disclosure Statement</b>  (37 CFR §1.98(b))	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 17109-013001 / 923	Application No. 10/658,355
	Applicant Rene Gantier et al.		
	Filing Date September 8, 2003	Group Art Unit 1631	

**U.S. Patent Documents**

Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	2004/0132977	07/08/04	Gantier et al.	530	351	09/08/03
	AB	2006/0195268	08/31/06	Vega	702	19	04/28/06
	AC	2006/0247170	11/02/06	Guyon et al.	514	12	06/26/06
	AD	2006/0251619	11/09/06	Borrelly et al.	424	85.6	05/04/06
	AE	2007/0172459	07/26/07	Gantier et al.	424	85.5	02/13/07

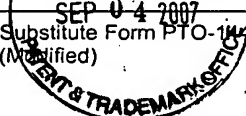
**Foreign Patent Documents or Published Foreign Patent Applications**

Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation	
							Yes	No
	AF	06/024547	03/09/06	PCT				

**Other Documents (include Author, Title, Date, and Place of Publication)**

Examiner Initial	Desig. ID	Document
	AG	Blazquez, J., et al., "Single amino acid replacements at positions altered in naturally occurring extended-spectrum TEM $\beta$ -lactamases," Antimicrobial Agents and Chemotherapy, 31(1):145-149, (1995).
	AH	Martin, P., "Beyond the Next Generation of Therapeutic proteins," 10/2006, <a href="http://www.biotech-online.com/artimg/a20062123243425.PDF">http://www.biotech-online.com/artimg/a20062123243425.PDF</a> (accessed on 01/11/07) (3 pgs).
	AI	Media Release: "In Vivo Studies Provide Hope for Orally Available Protein Therapeutics," Paris, France and Boston, Massachusetts (USA), 04/26/06, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=169343">http://www.prnewswire.co.uk/cgi/news/release?id=169343</a> (accessed on 01/08/07) (3 pgs).
	AJ	Media Release: "Nautilus Biotech and Angel Biotechnology Sign Agreement to Manufacture Belerofon(R) (Improved Alpha Interferon) for Phase I Clinical Trials," Paris, France and Northumberland, England, 12/06/04, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=135767">http://www.prnewswire.co.uk/cgi/news/release?id=135767</a> (accessed on 01/08/07) (2 pgs).
	AK	Media Release: "Nautilus Biotech and HanAll Pharmaceutical Announce License Agreement to Develop Three Nautilus Biotech Products in South Korea," Paris, France, 03/06/07, <a href="http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&amp;STORY=/www/story/03-06-2007/0004540099&amp;EDATE=">http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&amp;STORY=/www/story/03-06-2007/0004540099&amp;EDATE=</a> (accessed on 03/16/07) (3 pgs).
	AL	Media Release: "Nautilus Biotech announces IND filing for Belerofon®, its oral, long-lasting, Interferon-alpha drug," Paris, France, 02/07/07, <a href="http://www.nautilusbiotech.com/news_270207.html">http://www.nautilusbiotech.com/news_270207.html</a> (accessed on 03/16/07) (3 pgs).
	AM	Media Release: "Nautilus Biotech Announces IND Filing for its Injectable Long-Lasting INTERFERON-alpha, BELEROFON(R)," Paris, France, 10/10/06, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=181151">http://www.prnewswire.co.uk/cgi/news/release?id=181151</a> (accessed on 01/08/07) (2 pgs).

Examiner Signature	Date Considered
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

 <p><b>List of Patents and Publications for Applicant's Information Disclosure Statement</b></p> <p>(37 CFR §1.98(b))</p>	<p>U.S. Department of Commerce Patent and Trademark Office</p>	<p>Attorney's Docket No. 17109-013001 / 923</p>	<p>Application No. 10/658,355</p>
		<p>Applicant Rene Gantier et al.</p>	
		<p>Filing Date September 8, 2003</p>	<p>Group Art Unit 1631</p>

**Other Documents (include Author, Title, Date, and Place of Publication)**

Examiner Initial	Desig. ID	Document
	AN	Media Release: "Nautilus Biotech Announces Progress on Belerofon, an Improved IFNalpha With Single Amino Acid Sequence Change, Designed to Reduce Frequency of Injection for Hepatitis C Chronic Infection and Cancer," Paris, France, 03/23/04, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=119794">http://www.prnewswire.co.uk/cgi/news/release?id=119794</a> (accessed on 01/08/07) (2 pgs).
	AO	Media Release: "Nautilus Biotech Announces Progress on Improved Interferon Beta for Multiple Sclerosis," Paris, France, 02/27/04, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=118120">http://www.prnewswire.co.uk/cgi/news/release?id=118120</a> (accessed on 01/08/07) (1 pg).
	AP	Media Release: "Nautilus Biotech Announces Progress on Next-Generation Interferon Gamma," Paris, France, 04/25/05, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=144633">http://www.prnewswire.co.uk/cgi/news/release?id=144633</a> (accessed on 01/08/07) (1 pg).
	AQ	Media Release: "Nautilus Biotech Moves its Next-Generation Long-Lasting Interferon Beta into Regulatory Preclinical Development," Paris, France, 07/18/05, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=150268">http://www.prnewswire.co.uk/cgi/news/release?id=150268</a> (accessed on 01/08/07) (2 pgs).
	AR	Media Release: "Nautilus Biotech: 'Next Generation Biopharmaceuticals (NGB),' Paris, France, 06/21/04, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=125241">http://www.prnewswire.co.uk/cgi/news/release?id=125241</a> (accessed on 01/08/07) (1 pg).
	AS	Media Release: "Nautilus Moves its Long-Lasting, High Availability Human Growth Hormone Into Formal Preclinical Development," Paris, France, 01/09/06, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=161460">http://www.prnewswire.co.uk/cgi/news/release?id=161460</a> (accessed on 01/08/07) (2 pgs).
	AT	Media Release: "Nautilus Reaches its First Milestone in Collaboration With Serono on Next-Generation Human Growth Hormone," Paris, France, 02/22/05, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=140366">http://www.prnewswire.co.uk/cgi/news/release?id=140366</a> (accessed on 01/08/07) (1 pg).
	AU	Media Release: "Serono and Nautilus Biotech Sign Worldwide Agreement to Develop and Commercialize a Next-Generation Growth Hormone," Geneva, Switzerland and Paris, France, 11/15/04, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=134375">http://www.prnewswire.co.uk/cgi/news/release?id=134375</a> (accessed on 01/08/07) (2 pgs).
	AV	Media Release: "Wyeth Pharmaceuticals and Nautilus Biotech Announce Collaboration to Develop Hemophilia Therapies," 02/05/07, <a href="http://www.prnewswire.co.uk/cgi/news/release?id=189610">http://www.prnewswire.co.uk/cgi/news/release?id=189610</a> (accessed on 03/16/07) (2 pgs).
	AW	Media Release: "Nautilus Biotech announces IND filing for Belerofon <sup>®</sup> , its oral, long-lasting, Interferon-alpha drug," Paris, France, 02/27/07, <a href="http://www.nautilusbiotech.com/news_270207.html">http://www.nautilusbiotech.com/news_270207.html</a> (accessed on 03/16/07) (3 pgs).
	AX	Media Release: "Nautilus Biotech begins Phase I clinical trial in the USA for subcutaneous Belerofon <sup>®</sup> , its long-lasting, Interferon-alpha drug," Paris, France, 04/02/07, <a href="http://www.nautilusbiotech.com/news_020407.html">http://www.nautilusbiotech.com/news_020407.html</a> (accessed on 04/09/07) (3 pgs).
	AY	Media Release: "Nautilus Biotech and HanAll Pharmaceutical Announce License Agreement to Develop Three Nautilus Biotech Products in South Korea," Paris, France, 03/06/07, <a href="http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&amp;STORY=/www/story/03-06-2007/0004540099&amp;EDATE=">http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&amp;STORY=/www/story/03-06-2007/0004540099&amp;EDATE=</a> (accessed on 03/16/07) (3 pgs).
	AZ	Media Release: "Nautilus Biotech receives FDA approval for Phase I clinical trial in the USA for oral Belerofon <sup>®</sup> , its long-lasting, Interferon-alpha drug," Paris, France, 05/14/07, <a href="http://www.nautilusbiotech.com/news_100507.html">http://www.nautilusbiotech.com/news_100507.html</a> (accessed on 7/11/07) (3 pgs).

Examiner Signature	Date Considered
<p>EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	